PB91-213777

EPA Pesticide Fact Sheet No. 224: Uniconazole-P

(U.S.) Environmental Protection Agency, Washington, DC

3 Jul 91

U.S. Department of Commerce
National Technical Information Service
NTIS

50272-101

REPORT DOCUMENTATION PAGE | 1. REPORT NO. | 2. | PB91-213777

4. Title and Subtitle: EPA Pesticide Fact Sheets - UNICONAZOLE-P No. 224

5. Report Date: July 3, 1991

6.

7. Author(s): EPA, Office of Pesticide Programs, Registration Division

8. Performing Organization Rept. No.: 540/FS-91-138

9. Performing Organization Name and Address:
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division (H7505C)
401 M Street, SW
Washington, D.C. 20460

10. Project/Task/Work Unit No.

11. Contract(C) or Grant(G) No.
(C)
(G)

12. Sponsoring Organization Name and Address:
Same as #9

13. Type of Report & Period Covered

14.

15. Supplementary Notes

16. Abstract (Limit: 200 words)

This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. , A Fact Sheet is issued after one of the the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

17. Document Analysis a. Descriptors

Pesticides, regulations, Chemical Information Fact Sheet, Use Patterns, science findings.

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA 22161

18. Availability Statement:
Publicly Available

19. Security Class (This Report)
Unclassified

20. Security Class (This Page)
Unclassified

21. No. of Pages
8

22. Price

Environmental Protection Agency | and Toxic Substances (H7501C)

540/FS-91-138

PB91-213777

EPA

Pesticide Fact Sheet

Name of Chemical: Uniconazole-P
Reason for Issuance: New Chemical Registration
Date Issued: 7/3/91
Fact Sheet Number: 224

DESCRIPTION OF CHEMICAL

Generic Name: (E)-(+)-(S)-1-(4-Chlorophenyl)-4,4 dimethyl-2-(1,2,4-triazol-1-yl)pent-1-ene-3-ol

Common and Code Name: Uniconazole-P, S3307D

Trade and Other Names: Sumagic

EPA Shaughnessy Codes: 128976-8

Chemical Abstracts Service (CAS) Number: 83657-17-4

Year of Initial Registration: 1991

Pesticide Type: Herbicide/Plant Growth Regulator (PGR)

Chemical Family: Triazole

U.S. and Foreign Producers: Valent U.S.A. Corporation

USE PATTERNS AND FORMULATIONS

Application Sites: Greenhouse grown ornamentals

Types and Methods of Application: Sumagic is to be applied to a wide variety of greenhouse grown floriculture crops and container grown ornamentals. The method of application is foliar.

Application Rates: Rates vary depending upon species and variety of crop.

Formulations: 0.05% liquid

Mode of Action: Inhibition of gibberellin biosynthesis.

SCIENCE FINDINGS

SUMMARY SCIENCE STATEMENT

Review of the product chemistry, environmental fate, toxicology and ecological effects data has been completed. The available data support the conditional registration of Sumagic for the proposed use.

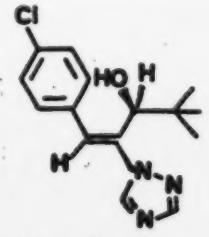
The HED Developmental/Reproductive Toxicity Peer Review Committee classified this chemical as a developmental toxicant. The classification was based on evidence which demonstrated increased incidence of cervical ribs in rats at non-maternally toxic levels and increased incidence of 14th ribs in rats at or above maternally toxic doses following intrauterine exposure to Uniconazole. This rat developmental toxicity study was classified core supplementary. For purposes of risk characterization, a tentative NOEL of 1 mg/kg/day for developmental toxicity will be used in estimating potential human risk. Using the tentative NOEL for developmental toxicity of 1 mg/kg/day and assuming 100% dermal penetration, the margins of exposure are estimated to be:

$[(1.0 \text{ mg/kg/day})/(4.1 \times 10^{-3} \text{ mg/kg/day})]$= 246 for the unprotected worker and;

$[(1.0 \text{ mg/kg/day})/(1.0 \times 10^{-3} \text{ mg/kg/day})]$= 1000 for the protected worker using rubber gloves as required on the label.

Chemical Characteristics of the Technical Material

N.R. - Not Required, N.A. - Not Applicable

	END USE PRODUCT (Sumagic)	TECHNICAL (Uniconazole)
Molecular Weight:		291.50
Molecular Formula:		$C_{15}H_{18}N_{3}OCl$
Chemical Structure:		
Color:	Colorless	white-light brown
Physical State:	Liquid emulsion	Crystalline powder

	END USE PRODUCT (Sumagic)	TECHNICAL (Uniconazole)
Odor:	Cyclohexanone-like	none
Melting Point:	N.R.	152.1 to 155 C
Boiling Point:	N.A.	N.A.
Density:	1.0049 gm/cm^3	1.284
Solubility:	N.R.	Organic solvents (w/v%) @ 20 C acetone 8.4 acetonitrile 1.6 n-hexane 0.02 chloroform 15.6 dimethyl-formamide 34.2 ethyl acetate 5.3 methanol 0.3 isopropanol 6.9 neochiozol 0.02
Vapor Pressure:	N.R.	4.0 x 10^{-5} mm Hg @ 20 C
Dissociation Constant:	N.R.	N.R.
Octanol/Water Partition Coefficient:	N.R.	Log P_{ow} 3.77
pH:	6.4 @ 20 C	5.7 @ 20 C
Stability:	N.R.	The TGAI is stable for 6 months @ 60 C
Oxidizing or Reducing Action:	Does not contain oxidizing or reducing agents.	
Flammability:	Not flammable	
Explodability:	Not explosive	
Storage Stability:	Decomposed less than 9% at 21 C for 15 months	Stable for 5 months at room temperature

	END USE PRODUCT (Sumagic)	TECHNICAL (Uniconazole)
Viscosity:	12.0 CPS @ 20 C	N.A.
Miscibility:	N.R.	N.R.
Corrosion Characteristics:	Not corrosive	Not corrosive
Dielectric Breakdown Voltage:	N.A.	N.A.

Toxicology Characteristics

Acute Testing	END USE PRODUCT (Sumagic)	TECHNICAL (Uniconazole)
Acute Oral:	LD_{50} > 5000 mg/kg Toxicity Category-IV	LD_{50} > 460-M,430-F mg/kg Toxicity Category-II
Acute Dermal:	LD_{50} > 5000 mg/kg Toxicity Category-III	LD_{50} > 2000 mg/kg Toxicity Category-III
Acute Inhalation:	LC_{50} > 5.9 mg/L Toxicity Category-IV	LC_{50} > 2.75 mg/L Toxicity Category-III
Primary Dermal Irritation:	Non-irritant Toxicity Category-IV	Non-irritant Toxicity Category-IV
Primary Eye Irritation:	Slightly Irritating Toxicity Category-III	Minimally irritating Toxicity Category-III
Dermal Sensitization:	Non-sensitizer	Non-sensitizer

Oncogenicity

In an 18-month mouse oncogenicity study, administration of Uniconazole to Crl:CD-1 mice at doses of 0, 10, 40, 200, or 1500 ppm (0, 1.5, 6, 30, and 225 mg/kg/day) resulted in a systemic NOEL of 30 mg/kg/day, and a LOEL of 225 mg/kg/day. These were based on increased absolute and relative liver weights in males, and increased relative liver weights in females, accompanied by focal chronic inflammation, necrosis, and pigmented macrophages. The HED Carcinogenicity Peer Review Committee evaluated the compound and classified Uniconazole as a Group C, possible human carcinogen. The classification was based upon an increased incidence of hepatocellular adenomas, carcinomas and adenomas/carcinomas combined in high dose male CD-1 mice. Quantification using the low dose extrapolation model ($Q1^*$) was not recommended because the tumor induced was primarily of benign nature, occurred only at the highest dose tested, and occurred in only

one sex of one species. Therefore, the Reference Dose (RFD) approach will be used for the estimation of potential human risk for future registrations involving food/feed uses.

A 2-year rat chronic/carcinogenicity study with rats fed doses of 0, 10, 40, 200 or 1000 ppm yielded a systemic NOEL of 200 ppm and an LOEL of 1000 ppm, respectively, and was based upon reduced body weight gain, increased centrilobular hepatocellular enlargement and vacuolization in males and females; increased relative liver weights and total cholesterol values. There was no evidence of carcinogenicity in the rat.

Subchronic Toxicity

A 90 day oral toxicity study with dogs fed doses of 0, 5, 20, 80, or 320 mg/kg/day yielded a systemic NOEL of 5 mg/kg/day and a LOEL of 20 mg/kg, respectively. These were based on decreased food consumption and body weight, increased SGPT and BSP retention, increased liver weights, heptocellular enlargement and cytoplasmic vacuolation of hepatocytes in animals administered 20 mg/kg/day and above.

A 90 day oral toxicity study with rats fed doses of 0, 30, 100, 1000, or 3000 ppm (approximate doses of male- 0, 2.25, 7.48, 73.0, 73.0, 228.0; female- 0, 2.24, 8.36, 79.0, 229.0 mg/kg/day) yielded a systemic NOEL of 100 ppm (10 mg/kg/day) and a LOAEL of 1000 ppm (100 mg/kg/day), respectively. These were based on increased liver weights in males and females, cloudy swelling of the liver (M,F), decreases in several hematology parameters (M,F), increased cholesterol and and phospholipid (F). In addition, at 3000 ppm, thyroid weights were increased (M), with increased incidence of small follicles and cytoplasmic vacuolation of the thyroid gland (M).

Chronic Toxicity

The requirement for a chronic oral dog study has been satisfied. The no-observed-effect-level (NOEL) is 2 mg/kg/day and was based upon increased liver weights in male dogs. Liver weight also was increased in male and female dogs at 20 mg/kg/day and correlated with hepatocellular enlargement, increased cytoplasmic homogeneity and increased bile pigment. The LOEL is 20 mg/kg/day and was based on increased liver weight.

Chronic Toxicity- Rodent (Refer to rat chronic/oncogenicity study above).

Developmental Toxicity

A rat developmental study using doses of 0, 1, 5, 25, and 50 mg/kg/day showed incidence of 14th rib increases at doses of 25 mg/kg/day and above. The incidence of cervical ribs increased in the 5, 25, and 50 mg/kg/day dose groups. The historical control data showed the cervical ribs to be an uncommon skeletal abnormality. This study was classified core-

supplementary because of the following: a. Inadequate historical control data concerning the cervical ribs b. Inadequate description of mating procedures including the method and rationale used to select the animals and the method employed for "culling" these animals and c. The term "tubercle of the liver" is unclear and needs to be defined. For purposes of risk characterization, a tentative NOEL of of 1 mg/kg/day for developmental toxicity will be used to determine the margin of exposure for potential human risk. A tentative LOEL of 5 mg/kg/day for developmental toxicity will be used based on increased evidence of cervical ribs development at 5 mg/kg/day. The NOEL for maternal toxicity is 5 mg/kg/day, while the LOEL for maternal toxicity is 25 mg/kg/day.

A rabbit developmental study using doses of 1, 3, 10, and 20 mg/kg/day of Uniconazole yielded a maternal NOEL of 10 mg/kg/day based on reduced food consumption and body weight gain during dosing. The developmental NOEL was 20 mg/kg/day (HDT). There were no treatment related increases in gross, visceral or skeletal abnormalities.

Reproduction

In a two generation reproduction study, rats were fed doses of 0, 15, 150, or 1500 ppm (daily doses of approximately 0, 0.72, 7.5, and 75 mg/kg/day). The NOEL for systemic toxicity is 7.5 mg/kg/day, based on increased liver weight, liver hypertrophy and vacuolization. The reproductive toxicity NOEL is 7.5 mg/kg/day, based on reduced pup weight during lactation. The LOEL was 75 mg/kg/day based on reduced pup body weight during lactatation. There was no other evidence of reproductive toxicity.

Mutagenicity Testing

No mutagenic activity was observed when tested in five strains (TA1535, TA1537, TA1538, TA98 and TA100) of Salmonella typhimurium or in E. coli with and without metabolic activation. The in vitro chromosomal aberration test indicated negative responses without activation at several concentrations of up to and including $2x10^{-4}$ M, but was positive when tested with activation at up to $3x10^{-4}$ M. In vitro testing in Chinese hamster ovary (CHO) cells was positive when tested with S-9 activation. Uniconazole tested slightly positive in DNA damage/repair assay and mouse activation micronucleus tests; however, these were graded unacceptable but upgradeable.

Environmental Characteristics

Hydrolysis - Hydrolysis studies of the (S)-(E)-isomer conducted at pH 5, 7 and 9 showed no degradation over a 30-day period.

Aerobic Soil Metabolism - Biodegradation is not an important degradation mechanism for Uniconazole. The half-life of Uniconazole in sandy loam soils is 390 days.

Mobility in soil - Uniconazole is very mobile in sandy loam and sand soils.

Volatility from soil - Uniconazole is not likely to volatilize from soil.

The Environmental Fate and Ground Water Branch (EFGWB) has determined that all the data requirements for greenhouse non-food use have been satisfied: hydrolysis, aerobic soil metabolism and mobility in soil (adsorption/desorption, column leaching). In summary, Uniconazole is characterized by the tendency of the compound to persist in aqueous media and in soils and for its leaching potential in soils of low organic matter content.

Ecological Characteristics			Classification
Avian acute toxicity:			
Bobwhite Quail	LD_{50}	1461 mg/kg	Practically
Mallard Duck	LD_{50}	> 2315 mg/kg	Non-toxic
Avian dietary toxicity:			
Bobwhite Quail	LC_{50}	> 5782 mg/kg	Slightly Toxic
Mallard Duck	LC_{50}	3442 mg/kg	Slightly Toxic
Freshwater fish acute toxicity:			
Bluegill Sunfish	LC_{50}	6.80 ppm	Slightly Toxic
Rainbow Trout	LC_{50}	14.8 ppm	Slightly Toxic

Available data indicate that the risk to avian and aquatic species will be minimal. Uniconazole is slightly toxic to birds on both an acute and dietary basis.

The Agency does not believe that conditional registration of this chemical will cause substantially greater adverse effects to the environment than other triazole products. Also, the labelled use pattern, greenhouse, lathhouse and shadehouses precludes environmental exposure.

Potential problems related to Endangered Species: No hazards are expected to endangered species.

Summary of Regulatory Positions

As conditions of registration, the registrant must submit additional information as listed below to upgrade the rat developmental study:

1. Historical control data concerning the phenomenon of 14th and cervical rib development.

2. A description of mating procedures including the method and rationale used to select the animals; and also the method employed for "culling" these animals.

3. A definition of the term "tubercle of the liver".

The registrant must submit also additional information to upgrade the rat unscheduled DNA synthesis and the mouse In vivo Micronucleus mutagenicity studies.

Required Unique Labeling

To protect against leaching and runoff, the following label-statements are being required:

"This product has the potential to leach into groundwater or to run off into surface water. In Greenhouses, Lathhouses or Shadehouses with soil flooring of high porosity and low organic content, do not apply directly to soil or to plants/pots in direct contact with soil"

For worker protection, the following labeling is required:

"Do not reenter treated areas until sprays have dried"

"Wear protective clothing, long sleeved shirt, and rubber gloves. Remove contaminated clothing and wash before reuse."

Summary of Major Data Gaps

The rat developmental study needs to be upgraded.
Two mutagenicity studies need upgraded.

CONTACT PERSON AT EPA

Robert J. Taylor
Product Manager (25)
Fungicide-Herbicide Branch
Registration Division (H7505C)
Office of Pesticide Programs
Environmental Protection Agency
401 M Street, S. W.
Washington, D. C. 20460

Office location and telephone number:

Room 245, Crystal Mall #2
1921 Jefferson Davis Highway
Arlington, VA 22202
(703) 557-1800

DISCLAIMER: The information in this Pesticide Fact Sheet is a summary only and is not to be used to satisfy data requirements for pesticide registration and reregistration. The complete Registration Standard for the pesticide may be obtained from the contact person listed above.